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TITLE: Prospective study of ALS mortality among World War II, Korea, and Vietnam Veterans

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14. ABSTRACT

We prospectively assessed the association between ALS mortality and self-reported military service in the American Cancer Society's Cancer Prevention Study II (CPS II) cohort, a cohort that includes over 500,000 men surveyed by questionnaire in 1982. ALS mortality was assessed via linkage with the National Death Index. Our original analyses(*3*) included ALS deaths (n=280) up to 1998. We have now extended the follow-up to 2002 (ALS deaths =513). Mantel-Haenszel relative risks (RR) adjusted for age and smoking were calculated and Cox proportional hazards models stratified on single year of age were used when adjusting for additional variables. Men who served in the military (69% of our population) had a significantly increased ALS mortality (RR=1.5) compared to those who did not serve. The increase in ALS mortality was similar among men who served in the Army or National Guard (RR=1.6), Navy (RR=1.7), or Air Force (RR=1.5). This increased risk of ALS appeared largely independent of the branch of service, years of service, and war periods during service. The project will continue as planned. We will extend the follow-up and examine the possible role of vitamin E supplements in prevention.

15. SUBJECT TERMS
Amyotrophic lateral sclerosis, military service, vitamin E, epidemiology

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Table of Contents

Introduction: Two recent studies suggested that the risk of Amyotrophic Lateral Sclerosis (ALS) is increased among Gulf War veterans.(*1, 2*) Initial work of ours suggested that military service prior to the Gulf War was also associated with an increase in risk for ALS.(*3*) Our purpose here was to extend our previous investigation by extending follow-up an extra 4 years to see whether the previous associations persisted.

Body: We prospectively assessed the association between ALS mortality and self-reported military service in the American Cancer Society's Cancer Prevention Study II (CPS II) cohort, a cohort that includes over 500,000 men surveyed by questionnaire in 1982. ALS mortality was assessed via linkage with the National Death Index. Our original analyses(*3*) included ALS deaths (n=280) up to 1998. We have now extended the follow-up to 2002 (ALS deaths =513). Mantel-Haenszel relative risks (RR) adjusted for age and smoking were calculated and Cox proportional hazards models stratified on single year of age were used when adjusting for additional variables. Men who served in the military (69% of our population) had a significantly increased ALS mortality (RR=1.5; 95% CI: 1.2-2.0; p = 0.0009) compared to those who did not serve. The increase in ALS mortality was similar among men who served in the Army or National Guard (RR=1.6), Navy (RR=1.7), or Air Force (RR=1.5). The increased risk of ALS did not vary much by years of service (figure 1), the number of major conflicts during service (figure 2), nor service specifically in World War 2, the Korean war, or the Vietnam war (figure3).

Key Research Accomplishments:

- We have completed the analyses of the extended follow-up of military service and risk of ALS death in the ACS CPS-II cohort through 2002.

Reportable Outcomes: Presentation of this work at the 22nd Neurotoxicology Conference in Raleigh Durham, September, 2005.

Conclusions: In extended analyses with almost twice as many ALS cases as our previous work, we confirmed an increased risk of ALS mortality among US military veterans who completed their period of service before the first Gulf War. This increased risk of ALS appeared largely independent of the branch of service, years of service, and war periods during service. The project will continue as planned. We will extend the follow-up and examine the possible role of vitamin E supplements in prevention.

References:

1. R. W. Haley, *Neurology* **61**, 750 (2003).
2. R. D. Horner *et al.*, *Neurology* **61**, 742 (2003).
3. M. G. Weisskopf *et al.*, *Neurology* **64**, 32 (Jan 11, 2005).

Figure 1. Relative risk of ALS by years of service, adjusted for smoking, education, alcohol intake, and vitamin E use.

Figure 2. Relative risk of ALS by number of major war periods during service, adjusted for smoking, education, alcohol intake, and vitamin E use.

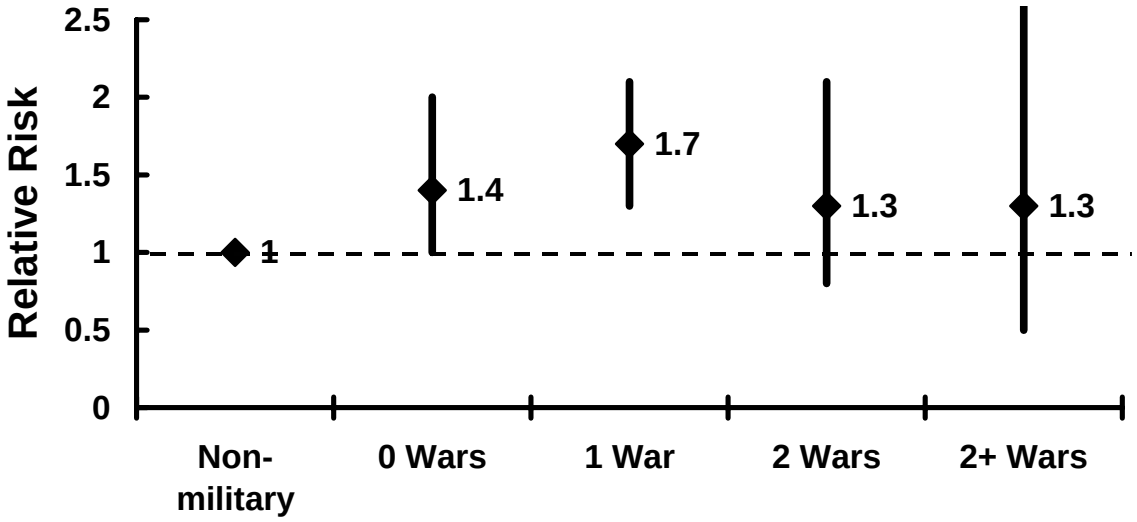

Figure 3. Relative risk of ALS by service during major war period, adjusted for smoking, education, alcohol intake, and vitamin E use.